

Appl. No. 09/520,130
Amendment dated April 18, 2005
Reply to Office Action of November 16, 2004

REMARKS/ARGUMENTS

Entry of the amendments and reconsideration of the claims in view of the following Remarks is respectfully requested.

Claims 47, 51, 54, 57, 59 and 62 have been amended merely for purposes of clarity. Applicants submit the amendments are supported throughout the specification including at page 23, lines 5-12. No new matter is added by the amendments. Claims 47-63 are pending in the application.

Petition for Extension of Time

It is noted that a two-month petition for extension of time is necessary to provide for the timeliness of the response. A request for such an extension is made extending the time for response from February 16, 2005 to April 16, 2005, which was a Saturday, which extends the time to respond to Monday, April 18, 2005.

Withdrawn Rejections

Applicants acknowledge the withdrawal of the rejection of claims 59-63 under 35 U.S.C. 103(a) over Ridgway, Carter (U.S. Pat. No. 5,807,706), or Carter (WO 96/27011) in view of Kostelney, and further in view of Vaughan.

Double Patenting

Claims 47-63 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-51 of copending Application No. 09/863,693. Claims 47-63 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39-49 of copending Application No. 09/373,403. Claims 47-63 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/143,437. As indicated in the previous Response, Applicants will consider filing a terminal disclaimer to overcome the double patenting rejections, if appropriate, upon notice of allowable claims.

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35 U.S.C. § 112, second paragraph

Claims 47-63 were rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 51 and 57, the Examiner contends it is unclear how an unaltered C_H3 domain may be a multimerization domain. Claims 51 and 57 have been amended to clarify that the C_H3 domain is altered by the presence of a non-naturally occurring disulfide bond.

Regarding claims 47 and 54, the Examiner states that the phrase "the bispecific antibody comprising" should be replaced with "wherein" and "which" should be deleted from elements (a) and (b). These claims have been amended in accordance with the Examiner's suggestions.

Regarding claim 59, the Examiner states that "common variable light chain domain" should be changed to "common light chain variable domain" to maintain consistency. Claim 59 has been amended in accordance with the Examiner's suggestion.

The Applicants submit that claims 47-63 are definite under 35 U.S.C. 112, second paragraph for the foregoing reasons. Withdrawal of the rejections is requested.

35 U.S.C. § 112, first paragraph

Claims 47-52 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The Examiner contends that the specification only teaches the use of the same light chain in all binding domains in the multispecific antibody. Applicants traverse this rejection.

The fundamental factual inquiry in whether the claims are sufficiently described "is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." *MPEP 2163 I.B.* Sufficient written description exists for a claim limitation if one of skill in the art can immediately discern the limitation from reading the original specification. *Waldemar Link, GmbH & Co. v. Osteonics Corp.*, 31 USPQ2d 1855 (Fed Cir. 1994). The specification need not, however, describe *ipsis verbis* what is recited in the claims; rather, the claim limitations may be supported in the specification through express, implicit, or inherent disclosure. *MPEP 2163 I.B.* Furthermore, Applicants need not disclose in detail what is conventional or well known to one of

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ordinary skill in the art. MPEP II 3(a). "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." *Id.*

Claims 47-52 recite a bispecific antibody comprising a first polypeptide and a second polypeptide, a first or second light chain variable domain chain each having three CDR regions, wherein the first and second light chain variable domains have at least 98% sequence identity, and only differ from one another at amino acid positions outside of the CDR regions. Applicants submit that one of skill in the art at the time of filing would have clearly understood from reading the specification that Applicants were in possession of the claimed bispecific antibodies at the time of filing.

Applicants' invention is directed to bispecific antibodies comprising binding domains for more than one antigen. Applicants have explicitly disclosed that paired light chains having at least 98% sequence identity can very likely be found for any V_L comparison (page 97, lincs 6-9). Applicants have disclosed the panning of a large human scFv antibody library for antibodies specific for eleven different antigens that represent considerable variation in structure and function (page 95, line 27 through page 96 line 9). After comparing the V_L sequences of the antibodies, Applicants discovered at least one, and often more than one, light chains having at least 98 % sequence identity for most pair wise comparisons (page 96, line 21 through page 97, line 26, Table 6, Appendix, Figure 4 and Figure 8). Based upon these results, it is likely that light chains that have at least 98% sequence identity can be found for any V_L comparison. These light chains were selected for binding to the specific antigen and, thus, could bind to the specific antigen of choice.

The Examiner contends, however, that the present specification does not contemplate bispecific antibodies comprising light chains having even 1 amino acid difference between them, because the specification allegedly only discloses comparing light chains to identify a single common light chain for use in a bispecific antibody.

The Applicants respectfully disagree, and submit that the specification suggests the use of light chains having less than 100% identity, for example, having at least 98% identity. The Examiner's attention is directed to page 97, line 24 to page 98, line 3. Here, the Applicants

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disclose two light chains that have 98% sequence identity and differ by two residues outside of the antigen binding CDRs. The specification states that these two amino acid changes may have little or no effect on antigen binding (page 97, lines 26-27). The specification concludes that, while the sequence similarity of these light chains makes them candidates for the common light chain of the invention, in an alternative embodiment "according to the invention, such light chains having 98-99% sequence identity with the light chain of a prospective paired scFv (Axl. 78, for example), *may be substituted with the paired light chain and retain binding specificity*" (page 97, line 28 through page 98, line 3) (emphasis added). Therefore, the present specification teaches that light chains having at least 98% sequence identity can be interchangeable in the design of bispecific antibodies of the invention, without having an effect on antigen binding. Applicants respectfully submit, therefore, that one of skill in the art would readily apprehend that Applicants were in possession of the concept of bispecific antibodies comprising light chains having at least 98% identity.

Applicants respectfully submit that claims 47-52 are amply described in the specification for at least the foregoing reasons. Furthermore, since the claims as amended are fully described by the specification, Applicants submit that no new matter was added by the amendments. Withdrawal of the rejection is respectfully requested.

Claims 59 and 61-63 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner contends that the specification only supports claims including a limitation that the differences between the sequences of the compared light chains occurs outside the CDRs. While Applicants do not acquiesce to the rejection, in order to expedite prosecution, Applicants have amended the claims. Applicants submit the claims as amended obviate the rejection and request withdrawal of this rejection.

Interview

Applicants request an interview with the Examiner and her supervisor to resolve any remaining issues with the application. Applicants' representative will contact the Examiner to schedule an interview.

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Summary

Applicants submit that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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